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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/551,341	04/18/2000	Clifford A. Brass	IN01023K	2066

24265 7590 03/27/2003

SCHERING-PLOUGH CORPORATION
PATENT DEPARTMENT (K-6-1, 1990)
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EXAMINER	
ANDRES, JANET L	
ART UNIT	**PAPER NUMBER**
1646	24

DATE MAILED: 03/27/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/551,341	BRASS ET AL.	
	Examiner	Art Unit	
	Janet L. Andres	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 January 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *7,8,10-19 and 47-54* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *7,8,10-19 and 47-54* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *23* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 27 January 2003 has been entered. The text of those sections of Title 35, U.S. Code, not included in this action can be found in a prior office action.

Claim Rejections - 35 USC § 103

2. Claims 7, 8, and 10-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over McHutchison et al. (New England Journal of Medicine, 1998, vol. 339, pages 1485-1492), Davis et al. (New England Journal of Medicine, 1998, vol. 339, pages 1493-1499), Poynard et al. (The Lancet, 1998, vol. 352, pages 1436-1422) or Reichard et al. (The Lancet, 1998, vol. 351, pages 83-87) in view of Abella et al. (Brit. J. Clin. Pharmacol., 1996, vol. 42, pages 731-747) and further in view of Sies et al. (Am. J. Clin Nutr., 1995, vol. 62, pp. 1315S-1321S). McHutchison et al., Davis et al., Poynard et al., and Reichard et al. each teach the use of interferon a-2b in combination with ribavirin to treat hepatitis C. Each further teaches treatment courses of 24-48 weeks, interferon doses of 3 MIU TIW and ribavirin doses of 600-1200 mg/day. These references, however, fail to teach antioxidants to treat ribavirin-induced hemolysis. Vitamin E as an inhibitor of hemolysis is taught by Abella et al. Abella et al. teaches Vitamin E as a "well-known antioxidant" (abstract) and teaches decreased hemolysis when Vitamin E is administered

(p. 740). Abella et al. fails to teach Vitamin E as an inhibitor of ribavirin-indiced hemolysis and does not teach Vitamin E derivatives or Vitamin C. Sies et al. teaches that Vitamin C, like Vitamin E, is an antioxidant (pp. 3-4 as printed) and thus it would be expected to have the same effects. Sies et al. does not teach the use of Vitamin C in combination with ribavirin. However, it would have been *prima facie* obvious to one of ordinary skill in the art, on reading the teachings of Abella et al. and Sies et al., to use Vitamin C or E to inhibit ribavirin-induced hemolysis . McHutchison et al., Davis et al., Poynard et al., and Reichard et al. each teach that this effect of ribavirin necessitated the reduction of ribavirin doses in several patients. One of ordinary skill would thus have been motivated to inhibit this hemolysis in order to maintain the desired dosage levels taught by each of these reports because each teaches that combination therapy is advantageous and that ribavirin was reduced or discontinued when hemolysis occurred. One of skill would predict, based on the teachings of Abella et al. combined with those of Sies et al., that Vitamin C and Vitamin E would be effective in this process and thus could be used to allow maintenance of ribavirin doses. To use Vitamin C and Vitamin E together would be obvious based on the fact that they have the same function: *In re Kerkhoven* (205 USPQ 1069, CCPA 1980) summarizes:

> "It is *prima facie* obvious to combine two compositions each of which is taught by prior art to be useful for the same purpose in order to form a combination that is to be used for the very same purpose: the idea of combining them flows logically from their having been individually taught in the prior art."

Further, it would have been *prima facie* obvious to one of ordinary skill in the art to use derivatives of Vitamin E directed to the same purpose, since one of ordinary skill would predict that they would have effects similar to the parent compound.

3. Claims 47-54 are rejected under 35 U.S.C. 103(a) as being unpatentable over McHutchison et al., Davis et al., Poynard et al. or Reichard et al. in view of Abella et al. and Sies et al. as applied to claims 7, 8, and 10-19 above, and further in view of U.S. patent 4917888 (Katre et al., 1990). McHutchison et al., Davis et al., Poynard et al., Reichard et al., and Abella et al. teach as set forth above but fail to teach pegylated interferons. Pegylation of proteins including interferons is taught by the '888 patent. It would have been *prima facie* obvious to one of ordinary skill in the art to use pegylated interferons in the regimes taught by McHutchison et al., Davis et al., Poynard et al., Reichard et al. because the '888 patent teaches that pegylation of interferons increases their physiological half life and their solubility at physiological pH (column 1, column 4).

In response to applicant's arguments against the references individually, on pages 3 and 4 of paper no. 22, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Applicant further argues that administration of Vitamin E alone was unsuccessful, and that the success with Vitamin C and Vitamin E together was thus unexpected. However, the specification as filed teaches neither the failure of Vitamin E alone or the unexpectedness of the success of the combination.

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –

> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

5. Claims 7, 8, 10-19, and 47-54 are rejected under 35 U.S.C. 102(e) as being anticipated by U.S. patent 6172046 (Albrecht et al. 2001).

The applied reference has a common assignee with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

The '046 patent teaches treatment of HCV with interferon α or pegylated interferon α in combination with ribavirin. See claims, columns 15 and 16. The '046 patent does not explicitly teach combination with Vitamin C and Vitamin E. However, no doses or treatment regimes are specified in the instant claims, and any patient treated by the methods of the '046 patent who was simultaneously taking a multivitamin would inherently have been treated as instantly claimed. Multivitamins contain both of these vitamins: see attached data from the Bayer Corporation. It is not necessary for the benefits of the administration of these vitamins to have been realized in order for such benefits to have occurred.

NO CLAIM IS ALLOWED.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet Andres, Ph.D., whose telephone number is (703) 305-0557. The examiner can normally be reached on Monday through Friday from 8:00 am to 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, Ph.D., can be reached at (703) 308-6564. The fax phone number for this group is (703) 872-9306 or (703) 872-9307 for after final communications.

Communications via internet mail regarding this application, other than those under U.S.C. 132 or which otherwise require a signature, may be used by the applicant and should be addressed to **[yvonne.eyler@uspto.gov]**.

All Internet email communications will be made of record in the application file. PTO employees do not engage in Internet communications where there exists a possibility that sensitive information could be identified or exchanged unless the record includes a properly signed express waiver of the confidentiality requirements of 35 U.S.C. 122. This is more clearly set forth in the Interim Internet Usage Policy published in the Official Gazette of the Patent and Trademark Office on February 25, 1997 at 1195 OG 89.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Janet Andres, Ph.D.
Patent Examiner

March 26, 2003